

224. In addition, where features or aspects of the invention are described in terms of Markush groups, those skilled in the art will recognize that the invention is also thereby described in terms of any individual member
5 or subgroup of members of the Markush group. For example, if X is described as selected from the group consisting of bromine, chlorine, and iodine, claims for X being bromine and claims for X being bromine and chlorine are fully described.

10 225. The invention has been described broadly and generically herein. Each of the narrower species and subgeneric groupings falling within the generic disclosure also form part of the invention. This includes the generic description of the invention with a proviso or
15 negative limitation removing any subject matter from the genus, regardless of whether or not the excised material is specifically recited herein.

226. Other embodiments are within the following claims.

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CLAIMS

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1. A modified exendin or exendin agonist comprising an exendin or exendin agonist linked to one or more polyethylene glycol polymers.
2. The modified exendin or exendin agonist of claim 1, wherein said exendin or exendin agonist is exendin-4.

3. The modified exendin or exendin agonist of claim 1, wherein said exendin or exendin agonist is linked to one polyethylene glycol polymer.
- 5 4. The modified exendin or exendin agonist of claim 1, wherein said exendin or exendin agonist is linked to two polyethylene glycol polymers.
- 10 5. The modified exendin or exendin agonist of claim 1, wherein said exendin or exendin agonist is linked to three polyethylene glycol polymers.
- 15 6. The modified exendin or exendin agonist of any one of claims 1-5, wherein said one or more polyethylene glycol polymers each have molecular weights between 500 and 20,000.
- 20 7. The modified exendin or exendin agonist of any one of claims 1-5, wherein said exendin or exendin agonist is linked to said one or more polyethylene glycol polymers through an epsilon amino group on a lysine amino acid of said exendin or exendin agonist.
- 25 8. The modified exendin or exendin agonist of claim 1, wherein said modified exendin or exendin agonist is selected from the group of compounds consisting of SEQ ID NOs. 211-240.
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9. The modified exendin or exendin agonist of claim 1, wherein said modified exendin or exendin agonist is selected from the group of compounds consisting of SEQ ID NOs. 219, 220, and 211.
- 5 10. The modified exendin or exendin agonist of claim 1, wherein said modified exendin or exendin agonist is selected from the group of compounds consisting of SEQ ID NOs. 211 and 212.
- 10 11. The modified exendin or exendin agonist of claim 1, wherein said modified exendin or exendin agonist is selected from the group of compounds consisting of SEQ ID NOs. 226 and 227.
- 15 12. The modified exendin or exendin agonist of claim 1, wherein said one or more polyethylene glycol polymers are linked to an amino, carboxyl, or thio group of said exendin or exendin agonist.
- 20 13. The modified exendin or exendin agonist of claim 1, wherein said one or more polyethylene glycol polymers are linked to the N or C termini, or the N and C termini of side chains of one or
- 25 more amino acids of said exendin or exendin agonist, wherein said amino acids are selected from the group consisting of lysine, aspartic acid, glutamic acid, and cysteine.

14. The modified exendin or exendin agonist of claim 1, wherein said one or more polyethylene glycol polymers are linked to said exendin or exendin agonist with one or more amino acid side chain moieties with amine or carboxylic groups, or amine and carboxylic groups.
15. A method of making a modified exendin or exendin agonist of claim 1, comprising linking said one or more polyethylene glycol polymer to said exendin or exendin agonist.
16. The method of claim 15, wherein said linking is performed by solid-phase synthesis.
17. A method of treating a disease benefited by administration of an exendin or exendin agonist, comprising the step of providing a modified exendin or exendin agonist of claim 1 to a patient having said disease and thereby treating said disease.
18. The method of claim 17, wherein said disease is selected from the group consisting of postprandial dumping syndrome, postprandial hyperglycemia, impaired glucose tolerance, a condition or disorder which can be alleviated by suppressing glucagon secretion, modulating triglyceride levels, reducing food intake, obesity, an eating disorder, insulin-resistance

syndrome, diabetes mellitus, a hyperglycemic condition, and a hypoglycemic condition.

- 5 19. A pharmaceutical composition comprising a modified exendin or exendin agonist of claim 1 and a pharmaceutically acceptable carrier.
- 10 20. A kit comprising a modified exendin or exendin agonist of claim 1 and instructions or packaging for use.
- 15 21. A method of beneficially regulating gastrointestinal motility in a subject comprising administering to said subject a therapeutically effective amount of a modified exendin or exendin agonist of claim 1.
- 20 22. A method of treatment for ingestion of a toxin comprising: (a) administering an amount of a modified exendin or exendin agonist of claim 1 effective to prevent or reduce the passage of stomach contents to the intestines; and (b) aspirating the contents of the stomach.
- 25 23. A method for reducing the appetite or weight, or lowering plasma lipids, of a subject comprising administering to said subject a therapeutically effective amount of a modified exendin or exendin agonist of claim 1.
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24. A method for modulating triglyceride levels in a subject, comprising administering to said subject a therapeutically effective amount of a modified exendin or exendin agonist of claim 1.

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25. A method for suppressing glucagon secretion in a subject, comprising administering to said subject a therapeutically effective amount of a modified exendin or exendin agonist of claim 1.

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26. A method for treating diabetes mellitus in a subject, comprising administering to said subject a therapeutically effective amount of a modified exendin or exendin agonist of claim 1.

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27. A method according to claim 26 wherein the diabetes mellitus is selected from the group consisting of Type 1 diabetes, Type 2 diabetes, and gestational diabetes.

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28. A pharmaceutical composition for use in the treatment of conditions or disorders associated with hypernutrition, or in reducing the appetite or weight of a subject, or in suppressing glucagon secretion, or in modulating triglyceride levels, or for use in lowering the plasma lipid level of a subject, comprising a therapeutically effective amount of a modified exendin or

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exendin agonist of claim 1 in association with a pharmaceutically acceptable carrier.

- 5 29. A modified exendin or exendin agonist comprising an exendin or exendin agonist linked to one or more molecular weight increasing compounds.
- 10 30. A modified exendin or exendin agonist according to claim 29 wherein at least one of the molecular weight increasing compounds is selected from the group consisting of a polyethylene glycol polymer, albumin, a polyamino acid, gelatin, succinyl-gelatin, poly((hydroxypropyl)methacrylamide), a fatty acid, a polysaccharide, a lipid amino acid, and dextran.
- 15 31. The use of a modified exendin or exendin agonist according to claim 30 for the preparation of a medicament.
- 20 32. A method of treatment of a subject comprising administering to said subject in need thereof a modified exendin or exendin agonist according to claim 30 in a pharmaceutically acceptable character.
- 25 33. A modified exendin or exendin agonist according to claim 29 which is a modified exendin-4.